

Food and Drug Administration Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Bridget Walton, MS, RAC Director, Regulatory Affairs Sunovion Pharmaceuticals, Inc. One Bridge Plaza, Suite 510 Fort Lee, NJ 07024

RE: NDA 200603

LATUDA® (lurasidone HCI) Tablets

MA #86

Dear Ms. Walton,

This letter notifies Sunovion Pharmaceuticals, Inc. (Sunovion) that the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has become aware of oral statements made by a Sunovion sales representative on May 17, 2011, to a healthcare professional regarding its drug, Latuda® (lurasidone HCI) tablets (Latuda). The sales representative's statements are false or misleading because they promote an unapproved use and minimize the risks associated with Latuda. Thus, this promotional activity misbrands Latuda in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(f)(1), (n).

Background

Below is a summary of the indication and most serious and most common risks associated with the use of Latuda.¹ According to its FDA-approved product labeling (PI) (in pertinent part):

Latuda is indicated for the treatment of patients with schizophrenia.

The PI for Latuda includes a Boxed Warning regarding increased mortality in elderly patients with dementia-related psychosis. Contraindications for Latuda include known hypersensitivity to lurasidone HCl or any components in the formulation, and strong CYP3A4 inhibitors and inducers. The PI also contains Warnings and Precautions regarding: cerebrovascular adverse reactions; neuroleptic malignant syndrome; tardive dyskinesia; metabolic changes, including hyperglycemia and diabetes mellitus, dyslipidemia, and weight gain; hyperprolactinemia; leukopenia, neutropenia, and agranulocytosis; orthostatic hypotension and syncope; seizures; potential for cognitive and motor impairment; and suicide.

Reference ID: 3058285

¹ This information is for background purposes only and does not necessarily represent the indication and risk information that should be included in the promotional activity cited in this letter.

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The most commonly reported adverse reactions for Latuda (incidence ≥5% and at least twice the rate of placebo) were somnolence, akathisia, nausea, parkinsonism, and agitation.

Promotion of Unapproved Uses

On Tuesday, May 17, 2011, at approximately 1:40 PM, a sales representative from Sunovion made a sales call to a psychiatrist at his office. During this sales call, the sales representative indicated that Latuda is only approved for schizophrenia use, but studies for use in bipolar disorder are being done and it is only a matter of time before it is approved for bipolar disorder. The sales representative continued the discussion of the unapproved use of Latuda for bipolar disorder by pointing out that two other psychiatrists in the area are using Latuda for the treatment of bipolar disorder, and both are pleased with the results in these patients. Overall, the sales representative spent a considerable amount of time during the sales call discussing the off-label use of Latuda in the treatment of bipolar disorder.

According to its PI, Latuda is only indicated for the treatment of patients with schizophrenia. Therefore, the oral statements made by the sales representative misbrand the drug by suggesting a new "intended use" for Latuda for which the PI lacks adequate directions for use. OPDP acknowledges that the sales representative stated that Latuda is only approved for schizophrenia and that use of Latuda for the treatment of bipolar disorder is off-label; however, these statements do not mitigate the misleading overall impression created by the sales representative during the sales call that Latuda is safe and effective for the treatment of bipolar disorder.

Minimization of Risk Information/Unsubstantiated Claim

During the sales call, the sales representative minimized the risk of common adverse reactions associated with Latuda treatment. For example, in this discussion, the sales representative indicated that somnolence can occur during the beginning of treatment; however, it usually goes away after a week. FDA is not aware of substantial evidence or substantial clinical experience to support this claim. The PI does not include any information indicating a decreased risk of somnolence over time. In fact, we note that the PI includes a WARNING AND PRECAUTION regarding the potential for cognitive and motor impairment, which states the following (in pertinent part):

LATUDA . . . has the potential to impair judgment, thinking or motor skills.

In short-term, placebo-controlled trials, somnolence was reported in 22.3% (224/1004) of patients treated with LATUDA compared to 9.9% (45/455) of placebo patients, respectively. The frequency of somnolence increases with dose; somnolence was reported in 26.5% (77/291) of patients receiving LATUDA 120 mg/day. In these short-

² See 21 CFR 201.100(c)(1); 21 CFR 201.128.

term trials, somnolence included: hypersomnia, hypersomnolence, sedation and somnolence.

Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that therapy with LATUDA does not affect them adversely.

Additionally, as noted in the ADVERSE REACTIONS section of the PI, somnolence was reported as one of the most common adverse reactions associated with the use of Latuda during clinical studies. If you have any evidence to support such claims, please submit it to the FDA for review.

Conclusion and Requested Action

For the reasons discussed above, the oral statements made by the Sunovion sales representative misbrand Latuda in violation of the FD&C Act, 21 U.S.C. 352(f)(1), (n).

OPDP requests that Sunovion immediately cease violative promotional activities/materials for Latuda such as those described above. Please submit a written response to this letter on or before December 28, 2011, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Latuda that contain violations such as those described above, and explaining your plan for discontinuing use of such violative materials. Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. Please note that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has been reorganized and elevated to the Office of Prescription Drug Promotion (OPDP). OPDP consists of the Immediate Office, the Division of Professional Promotion (DPP) and the Division of Direct-to-Consumer Promotion (DDTCP). To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP.

In addition, OPDP recently migrated to a different tracking system. Therefore, OPDP letters will now refer to MA numbers instead of MACMIS numbers. Please refer to MA# 86 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Latuda comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Jessica N. Cleck Derenick, PhD Regulatory Review Officer Division of Professional Promotion Office of Prescription Drug Promotion

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/s/ 	
JESSICA N CLECK DERENICK 12/14/2011	